Diffusion and MRS study of Huntington's Disease

L. Zhang[1], M. T. Lin[2], M. F. Beal[2], A. M. Ulug[1]

[1]Radiology, Weill Medical College of Cornell University, New York, NY, United States, [2]Neurology, Weill Medical College of Cornell University, New York, NY, United States

Introduction

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder characterized by motor, cognitive and emotional disturbances with onset ages between 35 and 50 years [1]. Death occurs 15 to 20 years on the average after symptoms appear. Atrophy of the brain, especially the caudate nucleus is the typical imaging finding [2]. Diagnosis of HD can be made by the direct triplet repeat gene test. MR diffusion and MR Spectroscopy (MRS) [3-5] are useful tools to quantify the changes of brain diffusion, levels of NAA, Cho, Cr or Lactate in HD patients.

Methods

21 HD patients (aged 19-58 years, average 44.5±9.1 years) and 15 age-matched normal volunteers (aged 29-59 years, average 39.1±10.1 years) were included in this study, 14 patients have both MRS and diffusion tensor study. Four patients were imaged longitudinally. The MR imaging was performed on a 1.5T clinical MR scanner with a quadrature head coil. Diffusion protocol parameters are: TR=10.5s, TE=100ms, matrix=128x128, slice thickness=5 mm, FOV=220 mm. Diffusion was measured in three orthogonal directions with b value of 1000s/mm^2. Single voxel PRESS MR Spectroscopy (MRS) was performed with TR=2s, TE=144ms. Two voxels were placed in area of calcarine fissure of the occipital lobe and left motor strip.

The D_{av} trace maps were calculated from the diffusion images. A computer C program was utilized to make diffusion histograms by distributing the pixels into 250 bins with a bin width of 0.02×10^{-5} cm^2/s [6]. This histogram was then fitted to a three compartment brain model. The mean of the brain tissue compartment is recognized as a mean diffusion constant for the entire brain (BD_{av}) and its the distribution width as σ. Using regions of interest, D_{av} was also measured in frontal lobe, thalamus and caudate.

Student *t*-test and Pearson correlation were used for statistical analysis of diffusion and MRS parameters. $P<0.05$ was set to be the significance threshold.

Results

The global diffusion parameters, BD_{av} and σ, and regional D_{av} of caudate are considerably higher in HD patients when compared to normal controls ($p<0.0001$, $p<0.001$, $p<0.05$, respectively). (Table 1).

Robust negative correlations were found between BD_{av} and NAA/H_2O and Cr/H_2O ratio in the left motor strip ($p<0.05$) (Figure 1). NAA/H_2O and Cr/H_2O ratios in the occipital lobe and the left motor strip have robust negative correlation to D_{av} measurement in the frontal lobe ($p<0.001$) (Figure 2, 3). Similar analysis revealed no correlation between BD_{av} and NAA/Cr or Cho/Cr ratio.

The NAA/H_2O and Cr/H_2O ratios in the occipital lobe robustly correlate to those in the left motor strip ($p<0.05$). Statistically, left motor strip has higher level of Cho/H_2O ($p<0.001$) and Cho/Cr ratio ($p<0.0001$) than the occipital gray matter.

Four patients had a repeated study over a period of 4 months. No statistical difference were found in the measured MRS and diffusion parameters between the two studies ($p>0.05$).

Discussion

The increased diffusion parameters in HD patients may suggest increased water content as well as gliosis and demyelination. The negative correlation of BD_{av} to NAA/H_2O suggests that the increased diffusion values are tied to the neuronal dysfunction. The robust correlation of NAA/H_2O and Cr/H_2O in the occipital lobe with those in the left motor strip suggests that the general neuronal and metabolism changes are in parallel and HD has a non-focal patho-physiology.

References

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Table 1. Diffusion measurements of HD patients and the normal controls (in 10^{-5}cm^2/s)

	BD_{av}	σ	D_{av} in caudate	D_{av} in frontal	D_{av} in thalamus
HD	0.778±0.033	0.189±0.016	0.866±0.213	0.801±0.201	0.737±0.168
normals	0.733±0.012	0.172±0.013	0.803±0.105	0.727±0.090	0.747±0.016
% increase	5.8%	8.9%	7.2%	9.3%	-1.4%
p value	<0.0001	<0.001	<0.05	>0.05	>0.05

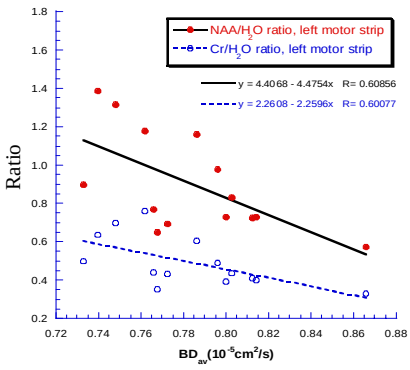

Fig. 1. BD_{av} has robust negative correlation to NAA/H_2O and Cr/H_2O ratio in the left motor strip.

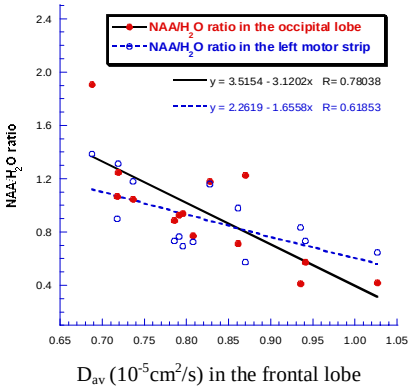

Fig. 2. Robust negative correlation between D_{av} in the frontal lobe and NAA/H_2O ratio in the left motor strip

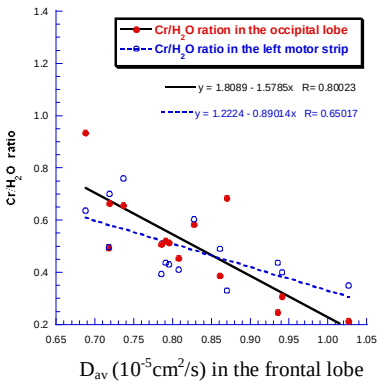

Fig. 3. Robust negative correlation between D_{av} in the frontal lobe and Cr/H_2O ratio in the left motor strip and occipital lobe.